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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,602	03/17/2005	Demetrio Manenti	GRT/3687-105	3448

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
04/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,602	MANENTI ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 11-13, 16-27* is/are rejected.

7)☒ Claim(s) *10,14 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 01/07/08.

The amendment filed 01/07/08 affects the application, 10/522,602 as follows:

1. Claims 1, 7, 8, 12, 13, 19-22, 25 have been amended.

2. New claims 26-27 have been added.

3. The responsive to applicants' arguments is contained herein below.

Claims 1-27 are pending in the application

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20, 21, 22, 25, 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites is indefinite since it is unclear how the derivative that is prepared can made to react with an organic compound to prepare the same derivative.

Claims 21, 22, 25, 26 provide for "a method of using a derivative or composition ……" but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 21, 22, 25, 26 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 9, 12, 13, 19, 23, 24, 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over FIDIA SPA (EP 0 555 898 A2).

In claim 1, applicant claims, a derivative formed between hyaluronic acid and at least one heterocyclic compound selected from purine or pyrimidine, said derivative having at least one bond of a ionic type between said acid and said at least one heterocyclic compound. Claims 2-6 are drawn to said derivative wherein the hyaluronic acid is of specific molecular weight. Claim 9 is drawn to said derivative involving specific ionic type between acid and heterocyclic compounds. Claims 12-13 and 27 are drawn to said derivative in association with at least one organic compound and wherein the organic compound is of specific type. Claims 23 and 24 are drawn to cosmetic or pharmaceutical compositions comprising said compounds.

FIDIA SPA discloses a medicament which comprises a partial or stoichiometrically neutral salt of hyaluronlc acid with a pharmacologically active substance of a basic nature (adenine arabinoside) (see claims 3 and 7; see also abstract). Furthermore, FIDIA SPA discloses that the hyaluronic acid used can have different molecular weights (see page 4, line 35 to page 5, line 31).

The difference between applicant's claimed derivative or composition and the derivative or composition of FIDIA SPA is that FIDIA SPA do not disclose the name of the derivative or compound. However, FIDIA SPA suggests a derivative or compound that read on the claimed invention (see claims 3 and 7; see also abstract).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have prepared any compound suggested by FIDIA SPA such as the neutral salt of hyaluronlc acid and a pharmacologically active substance such as adenine arabinoside, in order to use them to prepare medicaments such as antiviral or anti-tumor medicaments. It should be noted that neutral salt contain at least one ionic bond.

One having ordinary skill in the art would have been motivated, to prepare any compound suggested by FIDIA SPA with a reasonable expectation that the compounds would have the utility suggested by FIDIA SPA. Therefore one skilled in the art would have been motivated to make specific compounds suggested by FIDIA SPA, in order to use them to prepare medicaments such as antiviral or anti-tumor medicaments.

In claim 19, applicant claims a process for the preparation of a derivative from between hyaluronic acid and at least one heterocyclic compound according to Claim 1, characterized in

that hyaluronic acid or a salt thereof reacts with at least one heterocyclic compound in free or salified form.

FIDIA SPA discloses a process for the preparation of a derivative between hyaluronic acid and an active substance, characterized in that hyaluronic acid or a salt thereof is made to react with at least one heterocyclic compound in free or salified form. FIDIA SPA discloses that the hyaluronic acid salts with active substances can be prepared wherein all the carboxylic groups of hyaluronic acid may be salified or only a part of the groups are salified. In the partial salts, the remaining carboxylic groups of hyaluronic acid may be free or salified with other active substances (see page 15, lines 21-47). Furthermore, FIDIA SPA discloses the pharmacologically active substance can be the heterocyclic compound, adenine arabinoside (see claims 3 and 7; see also abstract).

The difference between applicant's claimed method and the method of FIDIA SPA is that FIDIA SPA do not exemplify the use of the heterocyclic compound, adenine arabinoside, per se. However, FIDIA SPA suggests a method for the preparation of a derivative or compound that read on the claimed invention (see page 15, lines 21-47; see claims 3 and 7; see also abstract).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the method of FIDIA SPA to prepare any compound suggested by FIDIA SPA such as the neutral salt of hyaluronlc acid and a pharmacologically active substance such as adenine arabinoside, in order to use them to prepare medicaments such as antiviral or anti-tumor medicaments.

One having ordinary skill in the art would have been motivated, to use the method of FIDIA SPA to prepare any compound suggested by FIDIA SPA with a reasonable expectation

that the compounds would have the utility suggested by FIDIA SPA. Therefore one skilled in the art would have been motivated to make specific compounds suggested by FIDIA SPA, in order to use them to prepare medicaments such as antiviral or anti-tumor medicaments.

Claims 1-9, 11, 12, 16, 17, 18, 23, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellini et al. (WO 00 01733)

In claim 1, applicant claims, a derivative formed between hyaluronic acid and at least one heterocyclic compound selected from purine or pyrimidine, said derivative having at least one bond of a ionic type between said acid and said at least one heterocyclic compound. Claims 1-6 are drawn to said derivative wherein the hyaluronic acid is of specific molecular weight. Claims 7 and 8 are drawn to said derivative wherein the heterocyclic compound is chosen from specific compounds including adenine. Claim 9 is drawn to said derivative involving specific ionic type between acid and heterocyclic compounds. Claim 11 is drawn to said derivative which is adenine hyaluronate. Claim 12 is drawn to said derivative in association with at least one different organic compound. Claims 16, 17 and 18 are drawn to said derivatives that are cross-linked. Claims 23 and 24 are drawn to cosmetic or pharmaceutical compositions comprising said compounds.

Bellini et al. disclose that the amide derivatives can be obtained by reaction of carboxyl or deacylated nitrogen of hyaluronic acid or a derivative thereof with an amine or with a pharmacologically active acid respectively, or they may be salified or simply associated with said compounds (see page 7, line 3 to page 8, line 14). Furthermore, Bellini et al. disclose that the pharmacologically active compounds can be made to react or be salified with the hyaluronic

acid include the heterocyclic compounds adenine, iodouridine and acyclovir (see page 7, line 3 to page 8, line 14, especially lines 25-27). It should be noted that salified compounds contain at least one ionic bond. Furthermore, Bellini et al. disclose that the hyaluronic acid derivatives can be cross-linked compounds wherein part or all of the carboxyl groups of the D-glucuronic residue form inner or inter-molecular esters with the alcoholic functions of the same polysaccharide chain or other chains respectively.

The difference between applicant's claimed derivative or composition and the derivative or composition of Bellini et al. is that Bellini et al. do not disclose a specific derivative or compound, per se. However, Bellini et al. suggests that hyaluronic acid can be made to react or salified with pharmacologically active compounds that are anti-virals or anti-tumorals such as the heterocyclic compounds adenine, iodouridine and acyclovir to form a hyaluronic acid derivative or compound (see page 7, line 3 to page 8, line 14, especially lines 25-27).

`It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have prepared any compound suggested by Bellini et al. such as the salt of hyaluronic acid and a pharmacologically active substance such as adenine, iodouridine and acyclovir, in order to use them as antiviral or anti-tumor agents.

One having ordinary skill in the art would have been motivated, to prepare any compound suggested by Bellini et al. with a reasonable expectation that the compounds would have the utility suggested by Bellini et al. Therefore one skilled in the art would have been motivated to make specific compounds suggested by Bellini et al., in order to use them as antiviral or anti-tumor agents. It should be noted that the use of hyaluronic acid of different

molecular weights depends on factors such as the type or severity of the tumor or viral condition that is to be treated with said derivative or compound.

Response to Arguments

Applicant's arguments with respect to claim 1-27 have been considered but are not found convincing.

The applicant argues that the '898 patent discloses a composition where two compounds must be present (i.e., Compound (1) and Compound (2)): Compound (1) being the pharmacologically active moiety and Compound (2) (hyaluronic acid or its salts) being the vehicle. However, FIDIA SPA (EP 0 555 898 A2) discloses that the hyaluronic acid salts with active substances can be prepared wherein all the carboxylic groups of hyaluronic acid may be salified or only a part of the groups are salified. In the partial salts, the remaining carboxylic groups of hyaluronic acid may be free or salified with other active substances (see page 15, lines 21-47). Furthermore, FIDIA SPA discloses the pharmacologically active substance can be the heterocyclic compound, adenine arabinoside (see claims 3 and 7; see also abstract). Furthermore, as set forth above, one having ordinary skill in the art would have been motivated, to use the method of FIDIA SPA to prepare any compound suggested by FIDIA SPA with a reasonable expectation that the compounds would have the utility suggested by FIDIA SPA. Therefore one skilled in the art would have been motivated to make specific compounds suggested by FIDIA SPA, in order to use them to prepare medicaments such as antiviral or anti-tumor medicaments. Also, it should be noted that the said vehicle (Compound (2) (hyaluronic acid or its salts) also has to be prepared before it can be used.

The applicant argues that with respect to the '898 patent, the present invention does not relate to the association of two separate components, because it does not necessitate of any pharmacologically active molecule to be joined with hyaluronic acid or its salt. The new hyaluronic acid salt according to the present invention, is already active in the cosmetic and/or pharmaceutical field. However applicant's derivative is formed between hyaluronic acid and a heterocyclic compound (purine or pyrimidine) wherein the derivative has at least one ionic bond; and consequently the said heterocyclic compound (purine or pyrimidine) does not exclude purines or pyrimidines that are pharmacologically active (which are salified to said hyaluronic acid). Furthermore, it should be noted that neutral salt contain at least one ionic bond.

The applicant argues that Bellini only discloses amide derivatives of hyaluronic acid. When it states that "they may be salified or simply associated with said compounds," it always refers to the already formed amide derivative (a covalent bond between hyaluronic acid and an amine derivative) and not to the hyaluronic acid itself. However, Bellini et al. disclose that the amide derivatives can be obtained by reaction of carboxyl or deacylated nitrogen of hyaluronic acid or a derivative thereof with an amine or with a pharmacologically active acid respectively, or they may be salified or simply associated with said compounds (see page 7, line 3 to page 8, line 14). Furthermore, Bellini et al. disclose that the pharmacologically active compounds can be made to react or be salified with the hyaluronic acid include the heterocyclic compounds adenine, iodouridine and acyclovir (see page 7, line 3 to page 8, line 14, especially lines 25-27). Also, it must be noted that Bellini et al.'s hyaluronic acid does not have to already be a formed amide derivative (see claim 1 of Bellini et al., which encompasses hyaluronic acid when $R_1 = R_2 = R_3 = R_4 = H$; R= OH and R_5 = acetyl; see also claim 8).

Allowable Subject Matter

Claims 10, 14, 15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Though the compound of the present invention are similar to the compounds of the prior art, the compounds of claim 10, 14 and 15 possess differences (e.g., structural) to the compounds of prior art documents and these differences are not suggested in the prior art, nor are obvious over the prior art.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be

reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry

April 26,, 2008.

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623